General

Guideline Title

Pharmacologic treatment of hypertension in adults aged 60 years or older to higher versus lower blood pressure targets: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians.

Bibliographic Source(s)

Qaseem A, Wilt TJ, Rich R, Humphrey LL, Frost J, Forciea MA. Pharmacologic treatment of hypertension in adults aged 60 years or older to higher versus lower blood pressure targets: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med. 2017 Mar 21;166(6):430-7. [49 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the overall quality of evidence (high, moderate, low, or insufficient evidence to determine net benefits or risks) and the strength of the recommendations (strong, weak) are provided at the end of the "Major Recommendations" field.

Recommendation 1: The American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) recommend that clinicians initiate treatment in adults aged 60 years or older with systolic blood pressure (SBP) persistently at or above 150 mm Hg to achieve a target SBP of less than 150 mm Hg to reduce the risk for mortality, stroke, and cardiac events. (Grade: strong recommendation, high-quality evidence). ACP and AAFP recommend that clinicians select the treatment goals for adults aged 60 years or older based on a periodic discussion of the benefits and harms of specific blood pressure (BP) targets with the patient.

High-quality evidence showed that treating hypertension in older adults to moderate targets (<150/90 mm Hg) reduces mortality (absolute risk reduction [ARR], 1.64), stroke (ARR, 1.13), and cardiac events (ARR, 1.25). Most benefits apply to such adults regardless of whether they have diabetes. The most consistent and greatest absolute benefit was shown in trials with a higher mean SBP at baseline (>160 mm Hg). Any additional benefit from aggressive BP control is small, with a lower magnitude of benefit and inconsistent results across outcomes.

Although this guideline did not specifically address pharmacologic versus nonpharmacologic treatments for hypertension, several nonpharmacologic treatment strategies are available for consideration. Effective nonpharmacologic options for reducing BP include such lifestyle modifications as weight loss, such dietary changes as the DASH (Dietary Approaches to Stop Hypertension) diet, and an increase in physical activity. Non-pharmacologic options are typically associated with fewer side effects than pharmacologic therapies and have other positive effects; ideally, they are included as the first therapy or used concurrently with drug therapy for most patients with hypertension. Effective pharmacologic options

include antihypertensive medications, such as thiazide-type diuretics (adverse effects include electrolyte disturbances, gastrointestinal discomfort, rashes and other allergic reactions, sexual dysfunction in men, photosensitivity reactions, and orthostatic hypotension), angiotensin-converting enzyme inhibitors (ACEIs) (adverse effects include cough and hyperkalemia), angiotensin-receptor blockers (ARBs) (adverse effects include dizziness, cough, and hyperkalemia), calcium-channel blockers (adverse effects include dizziness, headache, edema, and constipation), and beta-blockers (adverse effects include fatigue and sexual dysfunction).

Most of the included studies measured seated BP after 5 minutes of rest and used multiple readings. Clinicians should ensure that they are accurately measuring BP before beginning or changing treatment of hypertension. Assessment may include multiple measurements in clinical settings (for example, 2 to 3 readings separated by 1 minute in a seated patient who is resting alone in a room) or ambulatory or home monitoring.

Recommendation 2: ACP and AAFP recommend that clinicians consider initiating or intensifying pharmacologic treatment in adults aged 60 years or older with a history of stroke or transient ischemic attack to achieve a target SBP of less than 140 mm Hg to reduce the risk for recurrent stroke. (Grade: weak recommendation, moderate-quality evidence). ACP and AAFP recommend that clinicians select the treatment goals for adults aged 60 years or older based on a periodic discussion of the benefits and harms of specific BP targets with the patient.

Moderate-quality evidence showed that treating hypertension in older adults with previous transient ischemic attack (TIA) or stroke to an SBP target of 130 to 140 mm Hg reduces stroke recurrence (ARR, 3.02) compared with treatment to higher targets, with no statistically significant effect on cardiac events or all-cause mortality.

Recommendation 3: ACP and AAFP recommend that clinicians consider initiating or intensifying pharmacologic treatment in some adults aged 60 years or older at high cardiovascular risk, based on individualized assessment, to achieve a target SBP of less than 140 mm Hg to reduce the risk for stroke or cardiac events. (Grade: weak recommendation, low-quality evidence). ACP and AAFP recommend that clinicians select the treatment goals for adults aged 60 years or older based on a periodic discussion of the benefits and harms of specific BP targets with the patient.

An SBP target of less than 140 mm Hg is a reasonable goal for some patients with increased cardiovascular risk. The target depends on many factors unique to each patient, including comorbidity, medication burden, risk for adverse events, and cost. Clinicians should individually assess cardiovascular risk for patients. Generally, increased cardiovascular risk includes persons with known vascular disease, most patients with diabetes, older persons with chronic kidney disease with estimated glomerular filtration rate less than 45 mL/ min/1.73 m^2, those with metabolic syndrome (abdominal obesity, hypertension, diabetes, and dyslipidemia), and older persons. For example, among the included studies, SPRINT (Systolic Blood Pressure Intervention Trial) defined patients with increased cardiovascular risk as those meeting at least 1 of the following criteria: clinical or subclinical cardiovascular disease other than stroke; chronic kidney disease, excluding polycystic kidney disease, with an estimated glomerular filtration rate of 20 to less than 60 mL/min/1.73 m^2 of body surface area; 10-year risk for cardiovascular disease of 15% or greater based on the Framingham risk score; or age 75 years or older. This trial found that targeting SBP to less than 120 mm Hg compared with less than 140 mm Hg in adults without diabetes or prior stroke, at high-risk for cardiovascular disease, and with a baseline SBP of less than 140 mm Hg significantly reduced fatal and nonfatal cardiovascular events and all-cause mortality. In contrast, ACCORD (Action to Control Cardiovascular Risk in Diabetes) included only adults with type 2 diabetes and found no statistically significant reduction in the primary composite outcome of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular events (relative risk [RR], 0.94 [confidence interval (CI), 0.80 to 1.11]). This study did find a reduction in stroke events (RR, 0.58 [CI, 0.39 to 0.88]), but there were more serious adverse events associated with an SBP target of less than 120 mm Hg versus less than 140 mm Hg.

Definitions

Rating the Body of Evidence

- High = Further research is very unlikely to change confidence on the estimate of effect.
- Moderate = Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
- Low = Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
- Insufficient = Any estimate of effect is very uncertain.

The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak

Quality of Evidence	Strong	Strength of Recommendation	Weak
Low	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Insufficient evidence to determine net benefits or risks	Benefits Finely Balanced With Risks and Burden

*Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) workgroup.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Hypertension

Guideline Category

Treatment

Clinical Specialty

Cardiology

Family Practice

Geriatrics

Internal Medicine

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To present evidence-based recommendations on the benefits and harms of higher (<150 mm Hg) versus lower (≤140 mm Hg) systolic blood pressure (SBP) targets for the treatment of hypertension in adults aged 60 years or older

Target Population

Adults aged 60 years or older with hypertension

Interventions and Practices Considered

1. Establishing specific blood pressure (BP) targets (higher versus lower) based on patient risk factors and consideration of benefits and harms
2. Pharmacologic treatment

- Thiazide-type diuretics
- Angiotensin-converting enzyme inhibitors (ACEIs)
- Angiotensin-receptor blockers (ARBs)
- Calcium-channel blockers
- Beta-blockers

3. Non-pharmacologic treatment
    - Weight loss
    - Dietary changes (e.g., Dietary Approaches to Stop Hypertension [DASH] diet)
    - Increase in physical activity

Major Outcomes Considered

- All-cause mortality
- Morbidity and mortality related to stroke
- Cardiac events
- Harms

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was conducted by the Evidence-based Synthesis Program Center located at the Veterans Affairs Portland Health Care System, Portland, Oregon (see the "Availability of Companion Documents" field).

Data Sources and Searches

The investigators searched MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews, and ClinicalTrials.gov from database inception (refer to Appendix A in the systematic review supplement). The end search date for the larger report for the Veterans Health Administration was January 2015; the investigators updated the MEDLINE search in September 2016. They also examined the full text of all studies included in the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and the Blood Pressure Lowering Treatment Trialists' Collaboration.

Study Selection

The investigators reviewed titles and abstracts, and 2 independent reviewers evaluated the full articles for inclusion; disagreements were resolved through consensus. They included randomized trials of adults with a diagnosis of hypertension and mean age of at least 60 years that directly compared either 2 or more blood pressure (BP) targets or more versus less intensive antihypertensive therapy and that included 1 or more outcomes of interest (see detailed criteria in Appendix B in the systematic review supplement). Investigators excluded trials directly comparing antihypertensive drugs with one another and studies in populations with specific diagnoses in which medications were used primarily for effects other than BP lowering (for example, studies of beta-blockade in patients with systolic heart failure or studies of acute myocardial infarction). They included cohort studies that reported adverse effects associated with reductions in BP among patients receiving antihypertensive therapy.

Number of Source Documents

From 11,268 titles and abstracts, 330 articles were identified for full-text review. Forty-six publications representing 21 randomized, controlled trials and 3 cohort studies that contained primary data relevant to the key questions were included. A flow diagram of the literature yield and the disposition of included studies is presented in an Appendix Figure of the systematic literature review (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Rating the Body of Evidence

- High = Further research is very unlikely to change confidence on the estimate of effect.
- Moderate = Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
- Low = Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
- Insufficient = Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was conducted by the Evidence-based Synthesis Program Center located at the Veterans Affairs Portland Health Care System, Portland, Oregon (see the "Availability of Companion Documents" field).

Data Extraction and Quality Assessment

One investigator abstracted data elements from each study, and a second investigator reviewed entries for accuracy. Two reviewers independently assessed the quality of each trial using a tool developed by the Cochrane Collaboration. Disagreements were resolved through discussion. Each trial was given an overall summary assessment of low, high, or unclear risk of bias (see detailed criteria in Appendix C of the systematic review supplement).

Data Synthesis and Analysis

Primary effectiveness outcomes of interest were all-cause mortality, stroke (fatal or nonfatal), and cardiac events (myocardial infarction and sudden cardiac death), all after at least 6 months of treatment. The investigators examined the following harms: cognitive impairment, quality of life, falls, fractures, syncope, functional status, hypotension, acute kidney injury (defined as doubling of serum creatinine level or need for renal replacement therapy), medication burden, and withdrawal due to adverse events. The investigators did not specifically search for studies reporting well-known drug-specific adverse effects, such as angiotensin-converting enzyme inhibitor (ACEI)–induced cough or thiazide diuretic–induced hypokalemia, but they described common adverse events of intensive therapy leading to higher rates of withdrawal among trials. The overall strength of evidence for each outcome was classified after group discussion as high, moderate, low, or insufficient based on the consistency, coherence, and applicability of the body of evidence as well as the internal validity of individual studies.

The investigators conducted study-level meta-analyses to generate pooled estimates for each outcome after considering clinical and methodological diversity among studies. The profile-likelihood random-effects model was used to combine relative risks (RRs). They assessed the magnitude of statistical heterogeneity among studies using the standard Cochran chi-square test, the I^2 statistic. All analyses were performed using Stata/IC 13.1 (StataCorp).

Several sensitivity analyses were performed to help address the heterogeneity of study design and patient populations. Because studies with a

lower mean age were likely to include patients younger than 60 years, the investigators conducted separate analyses of studies with a mean population age of at least 70 years and studies with inclusion criteria stipulating entry age of at least 60 years to ensure that results were consistent. Studies were analyzed according to baseline blood pressure (BP) to compare treatment effects among patients with moderate to severe hypertension (systolic blood pressure [SBP] ≥160 mm Hg) versus those with mild hypertension (SBP <160 mm Hg), and the investigators analyzed studies according to achieved BP (SBP <140 mm Hg). They also conducted analyses with and without trials that achieved minimal between-group differences in SBP (≤3 mm Hg).

Trials specifically comparing BP targets of SBP less than 140 mm Hg or diastolic BP (DBP) of 85 mm Hg or lower versus higher targets were examined because these trials most directly address the incremental benefit of treatment intensification in mild hypertension. Finally, the investigators examined secondary prevention of stroke by examining BP treatment effects in studies of patients with prior stroke, but excluded those of acute management of stroke (<1 week).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The evidence review was conducted by the Portland VA Health Care System Evidence-based Synthesis Program to address the following key questions (KQs):

KQ1a: In adults aged 60 years or older, what are the health outcome effects of differing blood pressure (BP) targets?

KQ1b: In patients who have suffered a transient ischemic attack (TIA) or stroke, does treatment of BP to specific targets affect health outcomes?

KQ2: How does age modify the benefits of differing BP targets?

KQ3: How does the patient burden of comorbid conditions modify the benefits of differing BP targets?

KQ4: What are the harms of targeting lower BP in older patients? Do the harms vary with age?

KQ5: Do the harms of targeting lower BP vary with patient burden of comorbid conditions?

The guideline was jointly developed by the American College of Physicians' (ACP's) Clinical Guidelines Committee and representatives from the American Academy of Family Physicians (AAFP) according to ACP's guideline development process, details of which can be found in the methods paper (see the "Availability of Companion Documents" field). The committee used the evidence tables in the accompanying systematic review and full report (see the "Availability of Companion Documents" field) when reporting the evidence and graded the recommendations (see the "Rating Scheme for the Strength of the Recommendations" fields) using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) method.

Rating Scheme for the Strength of the Recommendations

The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

*Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) workgroup.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline had a peer-review process through the journal and was posted online for comments from American College of Physicians (ACP) Regents and Governors, who represent physician members at the national and international level. The guideline was also reviewed by members of American Academy of Family Physicians' (AAFP's) Commission on Health of the Public and Science.

This guideline was approved by the ACP Board of Regents on 16 July 2016 and by the AAFP Board of Directors on 20 July 2016.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Mortality, incidence of stroke, and cardiac events were all reduced with treatment.
- Treating to a lower blood pressure (BP) target did not further reduce mortality, quality of life, or functional status, but it did reduce the incidence of stroke and cardiac events.

Refer to the "Benefits of Treating Higher Versus Lower BP Targets in Older Adults" section of the original guideline document for additional information.

Potential Harms

- Increased withdrawals due to adverse events with higher vs. lower blood pressure (BP) targets
- Increased cough, hypotension, and risk for syncope with treating to lower vs. higher BP targets
- No difference between higher and lower BP targets for renal outcomes, cognitive outcomes, or falls and fractures

Adverse Effects

Some of the adverse effects associated with antihypertensive medications include (but are not limited to) the following:

- Thiazide-type diuretics: electrolyte disturbances, gastrointestinal discomfort, rashes and other allergic reactions, sexual dysfunction in men, photosensitivity reactions, and orthostatic hypotension
- Angiotensin-converting enzyme inhibitors (ACEIs): cough and hyperkalemia
- Angiotensin-receptor blockers (ARBs): dizziness, cough, and hyperkalemia
- Calcium-channel blockers: dizziness, headache, edema, and constipation
- Beta-blockers: fatigue and sexual dysfunction

Although electrolyte disturbances are a common adverse effect of hypertension treatment in clinical practice, data were not presented on these abnormalities in the evidence review. Drugs to treat hypertension have well-known adverse effects, including hypokalemia, hyperkalemia, hyponatremia, hypotension, dizziness, headache, edema, erectile dysfunction, and cough.

Refer to the "Harms of Higher Versus Lower BP Targets in Older Adults" section of the original guideline document for additional information.

Qualifying Statements

Qualifying Statements

- Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All American College of Physicians (ACP) clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.
- The authors of this article are responsible for its contents, including any clinical or treatment recommendations.
- Evidence for adults who are frail or those with multi-morbidity is limited.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Qaseem A, Wilt TJ, Rich R, Humphrey LL, Frost J, Forciea MA. Pharmacologic treatment of hypertension in adults aged 60 years or older to higher versus lower blood pressure targets: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med. 2017 Mar 21;166(6):430-7. [49 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Mar 21

Guideline Developer(s)

American Academy of Family Physicians - Medical Specialty Society

American College of Physicians - Medical Specialty Society

Source(s) of Funding

Financial support for the development of this guideline comes exclusively from the American College of Physicians (ACP) operating budget.

Guideline Committee

Clinical Guidelines Committee of the American College of Physicians

Commission on Health of the Public and Science of the American Academy of Family Physicians

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Financial Disclosures/Conflicts of Interest

Authors followed the policy regarding conflicts of interest described at www.annals.org/article.aspx?articleid =745942 . Disclosures can also be viewed at www.acponline .org/authors/icmje/ConflictOfInterestForms.do?msNum=M16 -1785 . All financial and intellectual disclosures of interest were declared and potential conflicts were discussed and managed. Drs. Boyd, Kansagara, and

Vijan participated in the discussion for this guideline, but they were recused from voting on the recommendations because of active indirect intellectual conflicts. Dr. Manaker participated in the discussion for this guideline but was recused from voting on the recommendations because of an active indirect financial conflict. A record of disclosures and management of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at www.acponline.org/clinical_information/guidelines/guidelines/conflicts_cgc.htm .

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Annals of Internal Medicine Web site .

Availability of Companion Documents

The following are available:

- Weiss J, Freeman M, Low A, Fu R, Kerfoot A, Paynter R, Motu'apuaka M, Kondo K, Kansagara Dl. Benefits and harms of intensive blood pressure treatment in adults aged 60 years or older: a systematic review and meta-analysis. Ann Intern Med. 2017 Mar 21;166:419-29. Available from the Annals of Internal Medicine Web site .
- Benefits and harms of intensive blood pressure treatment in adults aged 60 years or older: a systematic review and meta-analysis. Supplement. 2017. 38 p. Available from the Annals of Internal Medicine Web site .
- Weiss J, Kerfoot A, Freeman M, Motu'apuaka M, Fu R, Low A, Paynter R, Kondo K, Kansagara D. Benefits and harms of treating blood pressure in older adults: a systematic review and meta-analysis. VA ESP project no. 05-225. Washington (DC): Department of Veterans Affairs (US); 2016 Apr. 106 p. Available from the U.S. Department of Veterans Affairs Web site .
- Qaseem A, Snow V, Owens DK, Shekelle P. The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. Ann Intern Med. 2010 Aug 3;153(3):194-9. Available from the Annals of Internal Medicine Web site .

A continuing medical education (CME) activity is available from the Annals of Internal Medicine Web site .

Patient Resources

The following is available:

- Pharmacologic treatment of hypertension in adults aged 60 years or older to higher versus lower blood pressure targets. Summaries for patients. Ann Intern Med. 2017 Mar 21;166(6):1-26. Available from the Annals of Internal Medicine Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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